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Personalized Medicine on Muscinous Ovarian Cancer

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ABSTRACT
Ovarian cancer (OC), ranking third among gynecological cancers, poses a significant health concern with the worst prognosis and highest mortality rate. The global incidence, as per 2018 data, reached 295,414 cases, constituting 3.4% of women's cancer cases. The prevalence has notably risen in Asian countries, including Singapore and Indonesia. This report highlights two cases from Dr. M. Djamil, emphasizing the importance of personalized medicine (PM) in treating OC. PM, leveraging genomic information, aids in tailoring treatments for individual patients. The standard treatment involves cytoreductive surgical debulking and platinum-based chemotherapy. Notably, PM has shown promise in addressing specific genetic mutations, such as BRCA1 and BRCA2, prevalent in breast and ovarian tumors, enabling more targeted therapeutic approaches and enhancing treatment outcomes.

Keywords: ovarian cancer, ovarian, muscinous

INTRODUCTION

Ovarian cancer (OC) is the eighth leading cause of cancer death among women worldwide and the sixth in Mexico (Torre et al., 2017). The incidence of OC increases over the women's lives and about half of them are 63 years or older (Fairbrother et al., 2021). Ovarian cancer has the worst prognosis and highest mortality rate (Torre et al., 2018). Based on Globocan 2018 data, there were 295,414 cases of ovarian cancer, accounting for 3.4% of all cancer cases in women. The incidence of ovarian cancer has increased in many countries in Asia. In Singapore, ovarian cancer is the 5th most common cancer in women. A total of 5.4% of new cancer cases and 5.1% of all cancer deaths are women. The prevalence of ovarian cancer in Indonesia based on Globocan 2020 is 7% (14,896 patients).

Ovarian cancer is a heterogeneous group of neoplasms generally classified by type and degree of differentiation (tumor grade) (Kossaï et al., 2018). Early diagnosis is difficult because there are no characteristic signs or symptoms of the condition. In most cases, these malignancies are discovered after the disease has already spread beyond the pelvis (stages III-IV), with a survival rate of less than 20%.

Approximately 85-90% of malignant OC cases correspond to epithelial ovarian cancer, serous carcinoma (52%), clear cell carcinoma (6%), mucinous carcinoma (6%), endometrioid carcinoma Cancer can be divided into four different types. Cancer (10%) [3].

Standard initial management of epithelial OC consists of surgical staging, surgical debulking, and administration of chemotherapy (Kuroki & Guntupalli, 2020). Conventional chemotherapy is platinum/taxane therapy, but different classes of chemotherapeutic agents can be used depending on the type of OC and its molecular profile (Levit & Tang, 2021). Adverse side effects, resistance, and disease recurrence after chemotherapy are the main reasons for using targeted therapies. Personalized medicine (PM) is more likely to fight tumors effectively (Krzyszczyk et al., 2018).

Personalized medicine (PM) provides an individualized therapeutic opportunity to treat each patient by relying on “omic” tools to match the correct drug to the genomic signature of a particular pathogen. PM can help predict the best treatment options for any woman with OC.

In 2011, TCGA analyzed 489 high-grade severe OC tumor samples to decode the OC genome and identified significantly mutated genes: TP53 (96%), BRCA1 (9%), and BRCA2 (8%). revealed certain characteristics. The other six significantly associated genes were CSMD3, NF1, CDK12, FAT3, GABRA6, and RB1.

Extensive molecular profiling of patient tumors is accelerating the adoption of PM in oncology (Pishvaian et al., 2020). Analysis of gene activity patterns revealed that expression signatures of 108 genes were associated with poor patient survival (Festari et al., 2024). Specific molecular profiles such as specific genetic mutations, characteristic transcriptional patterns, and alterations in cell signaling pathways play a central role in the development of targeted therapies.

The National Human Genome Research Institute (NHGRI), a laboratory of the National Institutes of Health (NIH), uses PM to make medical decisions for disease prevention, diagnosis, and treatment. It is defined as a new medical practice that leads to. PM is also known as precision medicine, personalized medicine, stratified medicine, targeted medicine, and genomic medicine.

Before the Human Genome Project started (30 years ago), a decade and a half ago, the groundbreaking Genome Sequencing Project (HAB-S), in which one of his authors participated, was the breakthrough of genomic knowledge in the clinic. Potential value has been explored. Diagnostic tests of response to treatment use specific genomic traits to predict (Yin et al., 2022). This first translational study in genomics may have contributed to achieving the world record for sequencing the largest portion of the human genome corresponding to the growth hormone locus. It resides in the invention of a predictive test of response to recombinant growth hormone therapy based on polymerase chain reaction (PCR).

In recent years, PM has made great strides in the diagnosis and treatment of gynecologic cancers (Powell et al., 2023). Genetic background is known to play an important role in the development of OC. The National Cancer Institute's Genomic Data Commons data portal hosts a collection of 3,401 distinctive OC cases, of which only 64 (1.8%) correspond to Hispanic or Latino ethnicity. [8], indicating the need for such studies. Prime Minister's pledge to this nation.

PM has proven its worth in breast and ovarian tumors by matching each patient's genome with the right treatment (at the right dose) [8]. Women affected by these tumors often have mutations in the BRCA1 and BRCA2 genes. These genes produce tumor suppressor proteins that help repair damaged deoxyribonucleic acid (DNA), thereby ensuring the genetic stability of cells. However, when cancer cells carry mutated versions of these genes, they become more sensitive to anticancer drugs that act by damaging DNA, such as cisplatin. In this sense, agents aimed at inhibiting the only other remaining DNA repair mechanism, poly (ADP-ribose) polymerase (PARP), could arrest the growth of these BRCA-mutant cancer cells. is known. The advantage of BRCA

testing is that this approach can be used to identify the potential to effectively fight these cancers. AncestryDNA, Helix, and 23andMe are international biotech companies that offer BRCA tests, and companies like (Vitagenesis) in Mexico offer his BRCA test as a companion diagnostic. Other predictive biomarkers for molecular testing of OC include genes such as ATM, BRiP1, CHEK2, PALB2, RAD51C, and RAD51D.

METHODS

We report a case report of ovarian cancer treated at Dr. M. Djamil. Data were taken while the patient was in treatment.

RESULTS AND DISCUSSION

This case report reports 2 patients with a diagnosis of ovarian cancer. The first patient, Mrs. M, 51 years old, came with complaints of an enlarged stomach since 6 months before being admitted to the hospital. The second patient, Mrs. PA aged 14 years came with complaints of enlarged stomach since 6 months ago. The results of the ultrasound of the two patients showed the conclusion that the suspect ovarian cancer was suggestive of adenocarcinoma muscinous. Both patients underwent conservative laparotomy for surgical staging In this case, a conservative surgical staging laparotomy was performed. The standard treatment for ovarian cancer is maximal cytoreductive surgical debulking followed by platinum-based chemotherapy. Confirmation of the diagnosis, as well as staging of the disease is carried out during the operation. However, efforts should be made to determine the histologic type of the tumor, including grading. Staging assessment in surgical-pathological grade should be performed according to current FIGO recommendations.

Personalized medicine (PM) or precision medicine in oncology is an emerging approach to tumor treatment and prevention that takes into account inter- and intra-tumor variability in genes, tumor environment (immunity), and lifestyle and morbidity of each person diagnosed with cancer. PM has the potential to adapt therapy to tumor oncogenic triggers and modulate the tumor immune environment. Furthermore, PM aims to optimize tumor response, thereby accounting for therapy-induced toxicity for any given patient. PM can help predict the best treatment options for any woman with ovarian cancer. In 2011, TCGA deciphered the ovarian cancer genome by analyzing 489 samples of high-grade serious OC tumors and revealing certain signatures of the genes found to be significantly mutated: TP53 (96%), BRCA1 (9%) and BRCA2 (8%). The other six significant related genes were: CSMD3, NF1, CDK12, FAT3, GABRA6 and RB1.

PM by making it possible to match each patient's genome with the right treatment (at the right dose), has made the case for breast and ovarian tumors. Women with these tumors often carry mutations in the BRCA1 and BRCA2 genes. These genes produce tumor suppressor proteins that help repair damaged deoxyribonucleic acid (DNA) and thus ensure the genetic stability of cells. But when cancer cells carry a mutated version of this gene, they become more sensitive to anticancer agents that work by damaging DNA, such as cisplatin. In this sense, drugs directed to inhibit the only remaining DNA repair mechanism, poly (ADP ribose) polymerase (PARP), have been found to inhibit the growth of such BRCA-mutated cancer cells.

Complete surgical resection is the gold standard for all cases of mucinous ovarian cancer (MOC). Advanced disease is often treated with platinum-based adjuvant chemotherapy. However, they were mainly developed for the more common high-grade serous ovarian cancer,

and the therapeutic efficacy of MOC is low. More effective therapies are needed to treat late-stage and platinum-resistant tumors. However, traditional drug development and clinical trial paradigms present significant challenges for such rare diseases. New approaches are needed to support evidence-based treatment decisions, including: such as registry trials. Recently, a number of targeted therapies have emerged as viable therapeutic options for other cancers, and in some of these metabolisable tumor mutations have also been observed in MOC. Therefore, a promising alternative approach to benefit current MOC patients involves DNA sequencing to identify the unique mutational profile of tumors and enable matching with available targeting agents. Such a pipeline may include special clearances to administer drugs already approved for clinical use in other cancers to certain of his MOC patients, or for inclusion in existing ongoing clinical trials. Special permits may be included. B. Basket study including patients with tumors in different anatomic sites. The implementation of such personalized medicine is facilitated by improved preclinical models. Through clinical research collaborations, this model uses patients' own tumor cells to test different putative therapies prior to clinical administration, enabling selection of available therapies. A drug/s that maximizes the chances of cancer remission in each patient.[10]

CONCLUSION

Nowadays, cutting-edge molecular tools are part of routine health care and the forthcoming of cancer diagnostic by providing insights towards personalized therapy. Gynecological cancers can also benefit from these insights, especially OC, which represents a serious worldwide health problem in women because of its heterogeneous molecular composition and unavailable effective diagnosis. PM can improve diagnosis, prognosis and prediction in OC by stratifying patients according to their molecular profile.[11]

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